Understanding the **Immune System**

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Understanding the
Immune System

by Shakeer Ahmed

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Introduction

Coronavirus epidemic is spreading fast across the world and even developed countries are worst hit as lakhs of people infected from deadly virus. The new coronavirus is likely to keep spreading for at least another 18 months to two years—until 60% to 70% of the population has been infected, a team of longstanding pandemic experts predicted in a report (CIDRAP). To stop further spreading washing hands with soap for 20 seconds, maintaining 6-feet social distance, using mask while going out in public and practicing respiratory hygiene are good measures but above all one thing stands between you and deadly coronavirus, that is your Immune System. This lockdown time thought of renew (y)our understanding and the science behind human Immune System - the second most complex system in our body after the brain. Lets explore how Immune System protects us from diseases.

A note from the author

The purpose of this book is to provide everyone better understanding of human immune system. It explains how our immune system works what happens if it malfunctions. I hope this book has covered all aspects of immune system and how to strengthen immune system.

I would like to extend my sincere thanks to Mr. Sk. M. Subhani - Nutritionist for guiding me to kick-start this book & Dr. Jaheda Shaik, Pharm.D; CPD Certified Nutrition Therapist for her valuable inputs. I sincerely acknowledge all the online resources which have helped me in bringing this book.

- Shakeer Ahmed

* Information provided in this book is purely for knowledge and not to be taken as medicinal advice.

Immune System

The human body have a complete defence system, the immune system to resist the harmful invasion by pathogens. Pathogens are various kinds of micro-organisms (bacteria, viruses, fungi) in the environment that we live in that constantly invade the human body.

These micro-organisms can cause infect/sickness. However, we don't get sick all the time due to our immune system. The immune system consists of various types of cells and different proteins that kill the harmful invading micro-organisms and protect our body from disease.

The destruction of foreign pathogens and the process of protecting human body against diseases is known as immune response. The overall function of Immune System is to prevent or limit infection. When the immune system first recognizes the invasion of pathogens it responds to address the problem. If the immune response cannot be activated when there is sufficient need, problem is aroused like infections and other diseases. On the other hand when the immune response is activated without the real threat or is not felt of danger passes different problems arise such as allergic reactions and auto immune diseases.

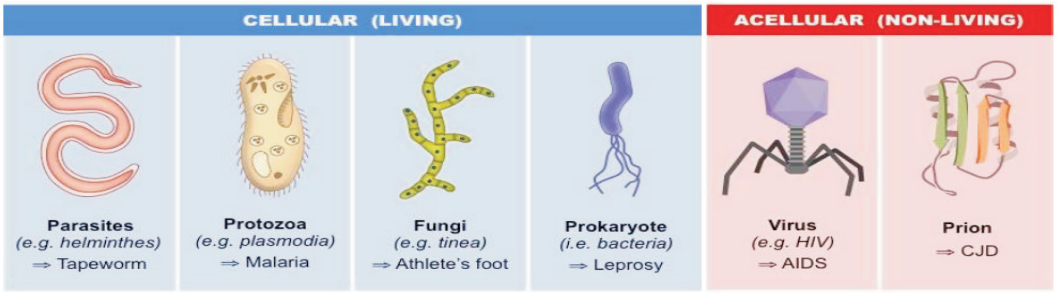
To understand how the immune system works in infection we need to know who the aggressors are. Potentially infectious agents include the following:

Viruses, which are non-living entities. Common examples are influenza virus, human immuno deficiency virus (HIV) and herpes simplex virus (HSV, which can cause cold sores or genital ulcers).

. Bacteria, are single-celled prokaryotic organisms. Examples include Staphylococcus and Streptococcus that cause acute infections such as abscesses and sore throats, and Mycobacteria that cause chronic infections such as tuberculosis and leprosy.

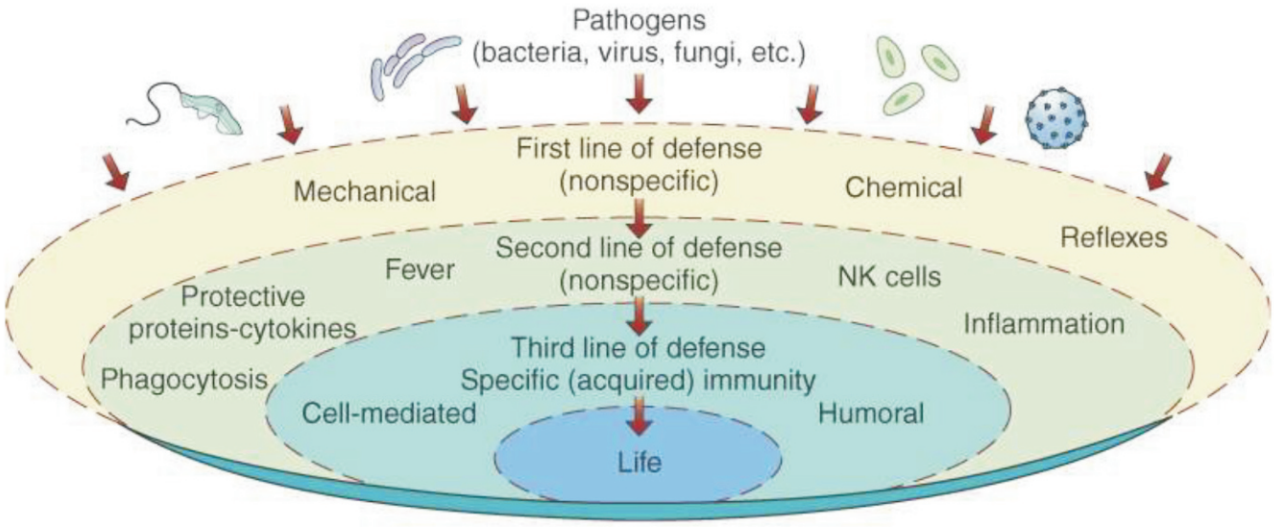
. Fungi, which are unicellular, such as Candida that causes thrush, or multicellular.

. Parasites, which are eukaryotic organisms. Some are single- celled protozoa that cause diseases such as malaria, others are large, multicellular organisms (metazoa) such as tapeworms.



Basic Structure of the Immune System

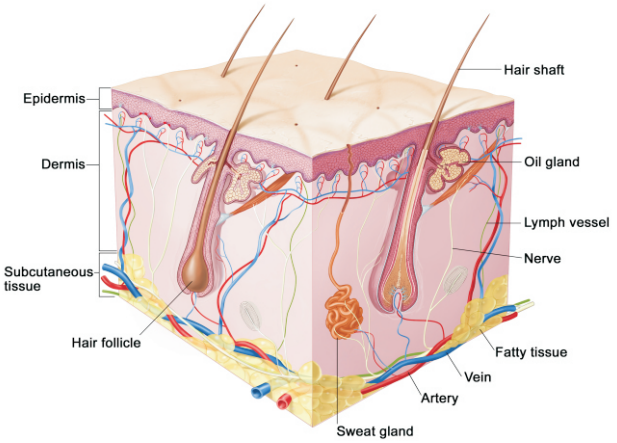
It consists of 3 layers of defense that protects our body from various types of attacks from micro organisms and even non living things like toxins, metals etc. Each layer consists of different mechanisms of immunity.



The first line of defence

The primary defence against infectious disease are the surface barriers that prevent pathogens from entering the body.

These surface barriers include intact skin (protect external boundaries) and mucous membranes (protect internal boundaries). The integrity of the skin is maintain with rapid blood clotting mechanism. If pathogens cannot enter the host body, they cannot disrupt normal physiological functions and cause disease.



Skin

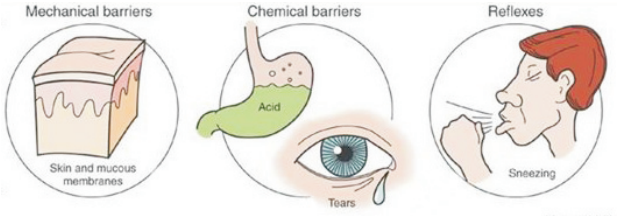
Skin is considered as largest organ of human body. The cornified layer (stratum corneum) on the outer layer of skin can resist the invasion of pathogens. Stratum corneum consisting layers of flattened of dead cells (corneocytes) with no nuclei and cell organelles. Fatty sebum and sweat (pH3.5) contain fatty acid that can kill germs.

Skin cells produce and secrete micro proteins that kill the invading microbes. The skin also contains immune cells helps to stop the microbes invading our body.

Blood clotting

When the skin is injured or torn, coagulation/clotting will be initiated. Blood clots will form rapidly at the wound to close the wound and stops pathogens from entering the human body

Similar type of barrier immunity is provided by other organs like respiratory system, gastro intestine, the geneto urinary system and the surface linings of our nose and larynx. All these types of surfaces provide physicall barrier and prevents the attacks from pathogens. They also provide chemica , anti microbial which try to stop the invading pathogens at very early stage.



Respiratory System

Mucous membrane in the respiratory tract secretes mucus to trap dust particles, spores and micro-organism.

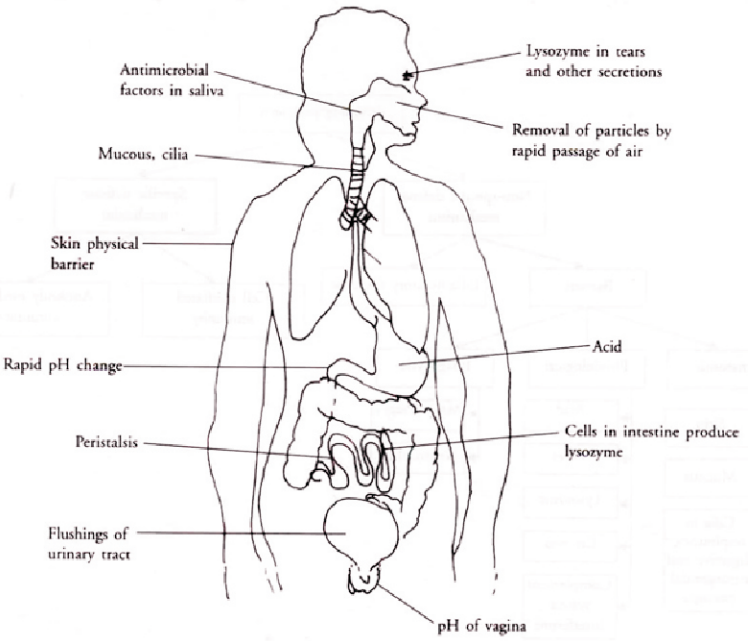
The mucus is removed by cilia of the tracheal ciliated epithelium. The cilia swipe the mucus towards the pharynx and is transported off in direction towards the mouth, where it is either swallowed or expelled via coughing.

Stomach

Our Stomach releases strong acids that kills most of the micro-organisms that will be accidentally injested while eating.

Other mucosa layer

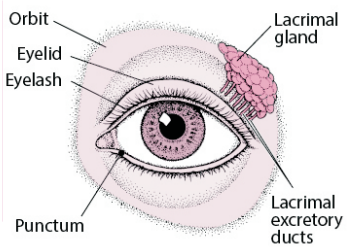
- The gastric mucosa secrets gastric acid (pH 1.5).
- The digestive tract secrets digestive enzymes such as peptidase, lipase and nucleotidase.
- Saliva and tears contain lysozyme
- The genital mucosa is bactericidal as well.



Non-specific defense mechanisms in the human body

Tears

The Tears in our eyes also contains special antimicrobial protins like lysozime that kill many pathogens. The constant flushing of tears also prevents any built up of foreign material in our eyes.



The second line of defence

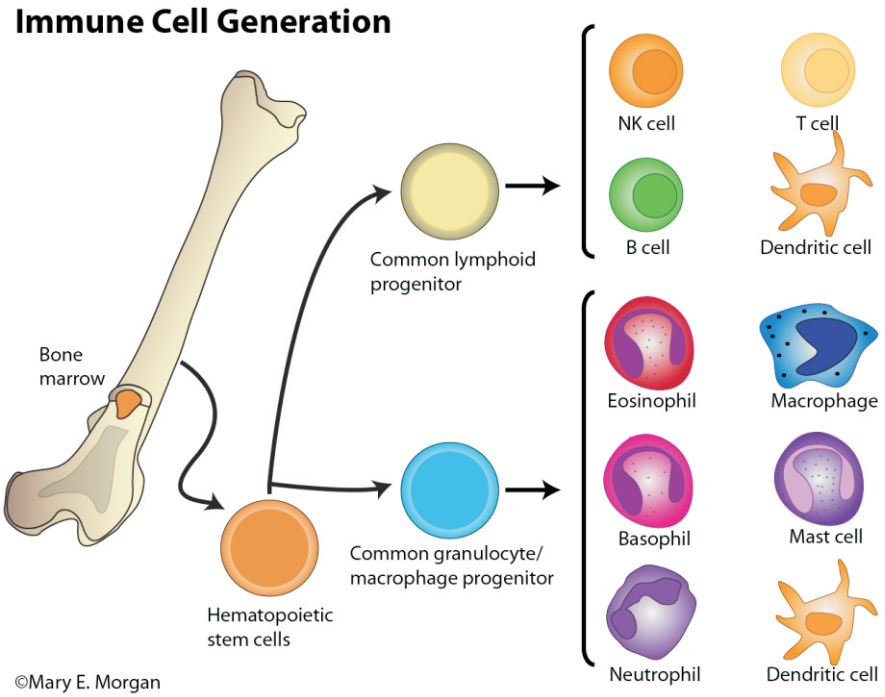
Sometime pathogens are able to break through the first line of defence and enter the body. The second line of defence - **Innate Immune System** is in place to stop these pathogens. It is already present in our body before birth. These defences are non-specific and do not differentiate between different types of pathogen and respond the same way upon every infection.

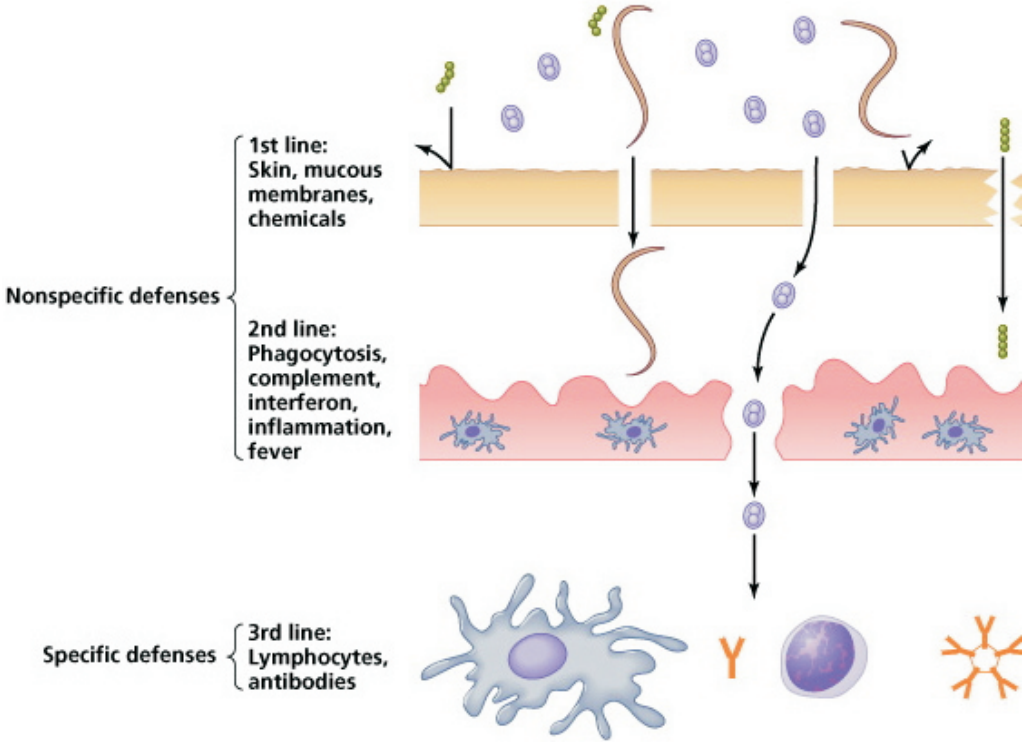
These includes: Innate Immune cells, Phagocytosis, Inflammation, Interferon and Fever.

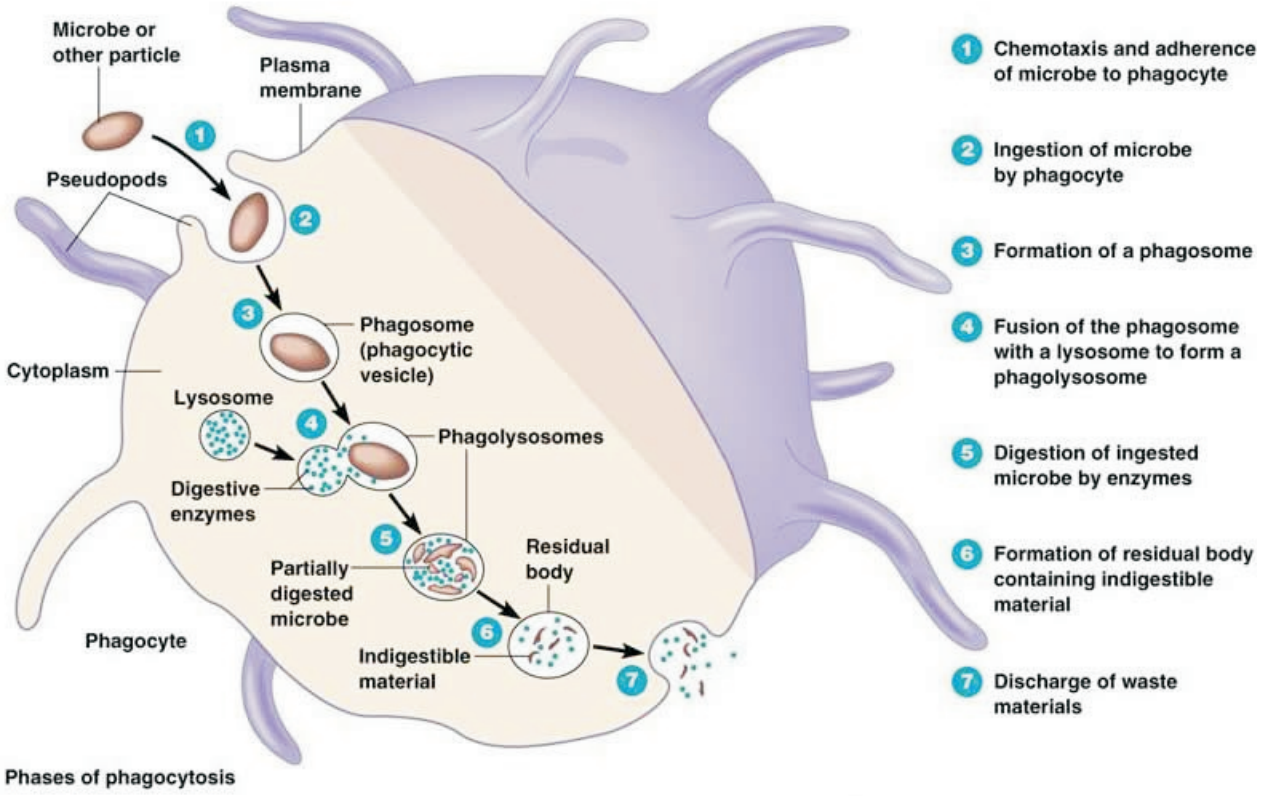
The defence system of innate immunity consist of the various types cells and the complement system.

The different types of cells in innate systems are Neutrophils, Mast cells, Basophils, Dendritic cells, Eosino cells, Monocytes, Macrophages and Natural Killer(NK) cells. All these cells are type of white blood cells or WBCs also known as Leukocytes (Leuko meaning white, cyte mean cell).

The Neutrophils are most abundant immune cells. Making up about to 60-70% of total populations of immune cells. They form an essential part of innate immune system.







Phases of phagocytosis

Phagocytosis

Phagocytes (phagocytic leukocytes) migrate to infection sites and engulf foreign bodies.
Phagocytes use enzymes such as Lysozyme to break down the pathogens.
Types of phagocytes:
• Monocytes (Macrophages)
• Neutrophil
• Basophil, Eosinophil etc.

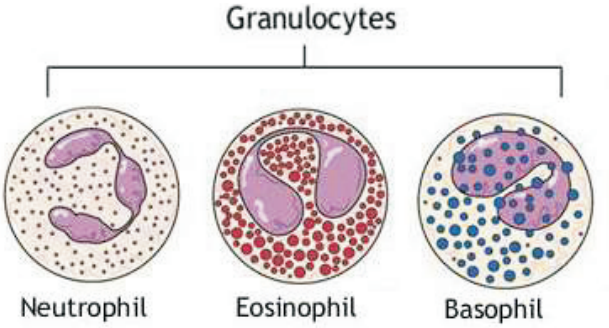
Phagocytosis (Phago-eating, cytosis-cell) in simple term cell eating.

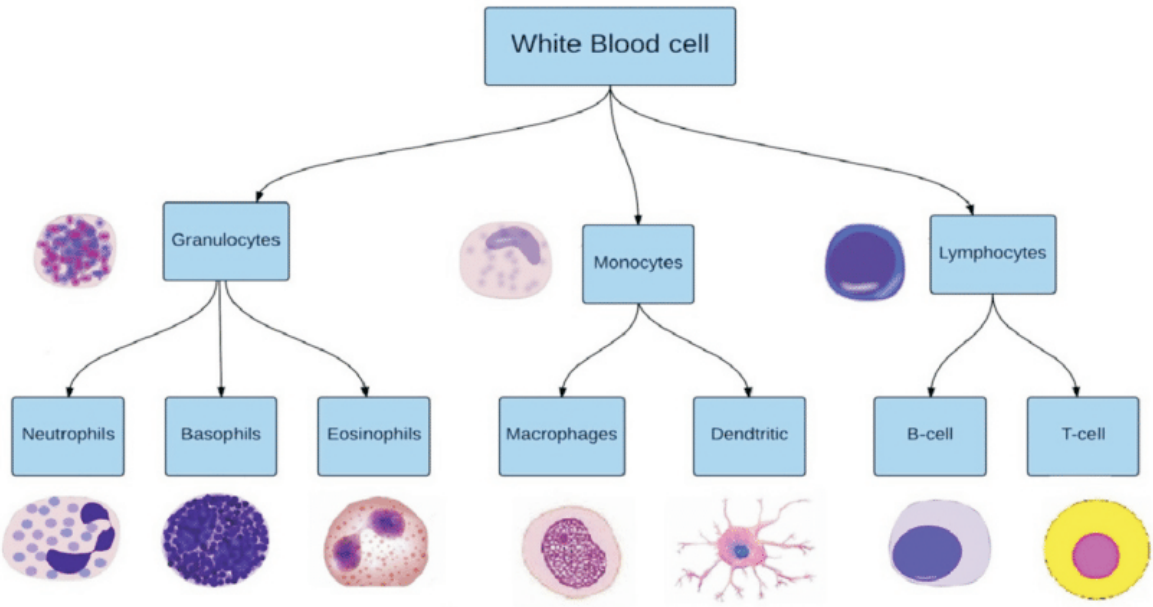
Granulocytes - a circulating White Blood Cell having prominent granules in the cytoplasm and a nucleus of two or more lobes are another kind of immune cell. They contain granules filled with potent chemicals, which allow the granulocytes to destroy micro-organisms. Neutrophils, Eosinophils and Basophils are granulocytes.

Neutrophils: These are found in blood stream, can enter parts of tissue where other cells/molecules cannot. These are a type of phagocytes that detect and eat the pathogens. Within the cell the neutrophils release various enzymes that kill and digest the pathogen. Neutrophils are one of the first responders of inflammatory cells to migrate toward the site of inflammation. They migrate through the blood vessels and then through interstitial tissue, following chemical signals in a process called chemotaxis.

Eosinophils: These also similar to neutrophils but usually have 2 lobes in nucleus, hence named as goggle shaped nucleus. Eosinophils make up about 1–3% of white blood cells. They develop in the bone marrow and are released into the bloodstream as neutrophils are, eosinophils reside in tissue. They are found in the medulla and the junction between the cortex and medulla of the thymus, and, in the lower gastrointestinal tract, ovaries, uterus, spleen, and lymph nodes, but not in the lungs, skin, esophagus, or some other internal organs under normal conditions. The presence of eosinophils in these latter organs is associated with disease.

Basophils: These are a type of white blood cell representing about 0.5-1% of circulating WBC. They arise and mature in bone marrow. Basophils appear in many specific kinds of inflammatory reactions, particularly those that cause allergic symptoms. Basophils contain anticoagulant heparin, which prevents blood from clotting too quickly. They also contain the vasodilator histamine, which promotes blood flow to tissues.





Mast Cells: These are a type of innate immune cells that reside in connective tissue and mucous membranes like the lining of our respiratory and gastrointestinal system. Mast cells are associated with wound healing and defense against pathogens. Often associated with allergy and anaphylaxis which has serious allergic reactions that can cause death. Mast cells contains granules containg abundant quantity of histamine and heparin. Histamin dilates blood vessels, which produces the characteristic inflammation and recruites nuetrophils and macrophages. They also help to link innate and adaptive immunity to fight against pathogens

Macrophage: Macrophages (meaning large eaters (greek)) are large phagocytic cells. Which are able to move out of the vascular system by migrating across the walls of blood vessels and entering the areas between the cells in pursuit of invading pathogens

Agranulocytes are white blood cells with a one-lobed nucleus and no granules in their cytoplasm. There are two types of agranulocytes Lymphocyte and Monocyte.

Monocyte: similar type to circulate in blood are monocytes. This is the cell with one lobed nucleus. In monocyte and macrophage the nucleus is round to oval with one lobe. The binding of killing molecule with the receptors on the surface of the macrophage triggers it to engulf and destroy the bacteria through the generation of reactive oxygen species. Pathogens also stimulate macrophage to produce chemokines which has special chemicals that attract other immune cells to side of infection.

Dendritic Cell: The word dendrite means branch and these cells has branch like structure these are present in those tissues that are in contact with external environment such as skin and inner lining of nose , lungs , stomach and intestine. The Dendritic cells are type of antigen presenting cells.

Antigen presenting cells detect the pathogens and create the antigens on the surface of the pathogens to limphocytes. Lymphocytes are cells of adaptive immunity. The dendritic cells present these antigens to lymphocytes and this leads to attack on pathogens by these lymphocytes and the antibodies they produce. So they are known as antigen presenting cells and present the antigen to lymphocyte. Dendritic cells also known as 'Langerhan Cells' after the scientist who discovered them. Type 1 interferons created mainly by dendritic cells play a central role in body's self defence against viruses.

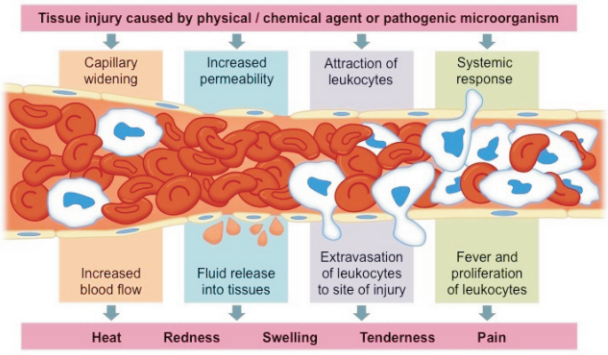
Natural Killer Cell: These are called NK Cells, are components of innate immune system that does not directly attach the invading microbes rather NK cells destroy our own cells that are become defective such as tumor cells and virus infected cells.

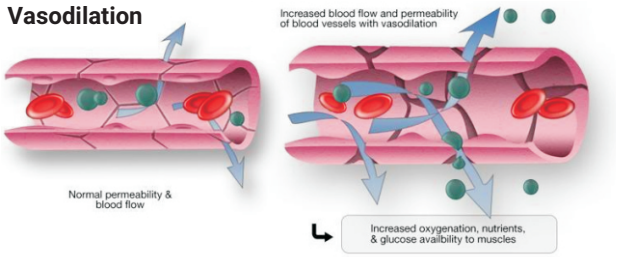
Innate immune system also has special type of defense mechanism known as – **complement system**. The complement system is set of about 20 proteins and it is known as complement the action of antibodies and other cells in destroying the pathogens and the complement system helps the antibodies and other immune cells to destroy the pathogens. The basic mechanism of action of complement system is as follows: When ever any pathogen enters our body it gets recognized by antibodies present in our blood. The binding of antibody to the pathogen is the most important factor for the activation of complement system, after it is activated a cascade of different enzymes act on the surface of the microbes to kill it.

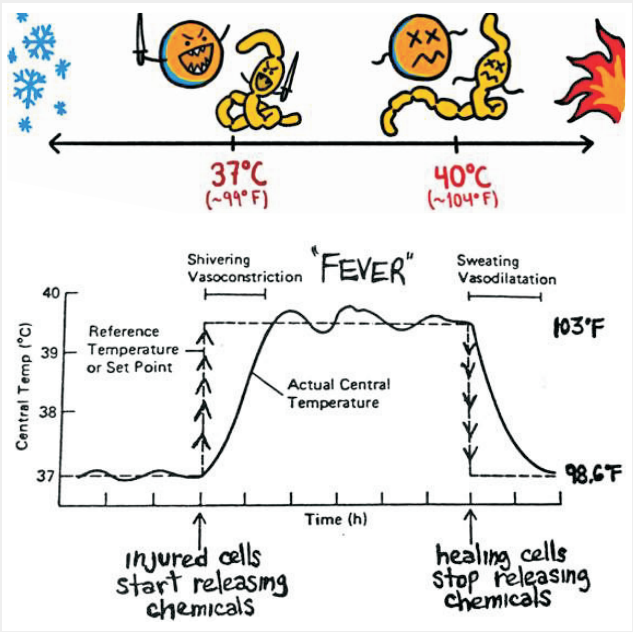
Inflammation

The inflammatory response is the non-specific way in which the body responds when a pathogen damages body tissue.

When tissue damage occurs, mast cells (localised) and basophils (circulating) release a chemical called histamine. Histamine causes local vasodilation and increases capillary permeability to improve the recruitment of leukocytes to the region. This allows more blood to flow to site of infection and bring along phagocytes and tissue fluids. This lead to localized swelling and pain (caused by the pressing of the nerves). Blood also brings heat from the body core, leading to increase local temperature to activate heat-shock proteins and suppress microbial growth and propagation.
Inflammation can be either short-term (acute) or long-term (chronic).







Fever

A fever is an abnormally high temperature associated with infection and is triggered by the release of prostaglandins.

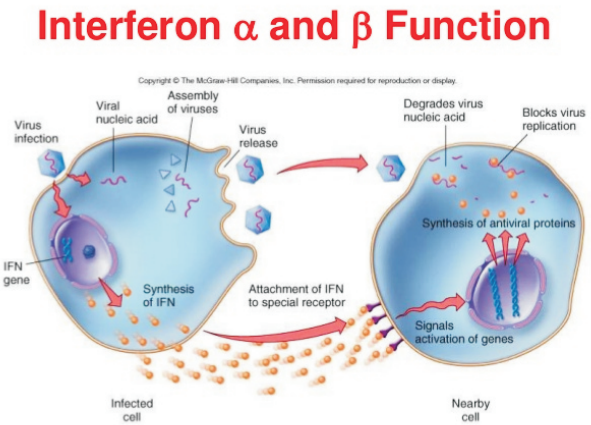
Fever may help to combat infection by reducing the growth rate of microbes (via the inactivation of microbial enzymes). It may also increase metabolic activity in body cells and activate heat shock proteins to strengthen the immune response.

Fever occurs when activated leukocytes release pro-inflammatory chemicals called cytokines. Cytokines stimulate the anterior hypothalamus to produce prostaglandins, which lead to an increase in body temperature. Up to a certain point a fever may be beneficial, but beyond a tolerable limit it can cause damage to the body's own enzymes.

Interferon

A group of proteins released by infected host cells in response to the presence viruses and other pathogens.

Interferons will bind to neighbouring cells and trigger antiviral responses in neighboring cells. Interferons produced in response to one virus will protect against many other types of viruses, and for this reason, interferon is considered a nonspecific form of defence.

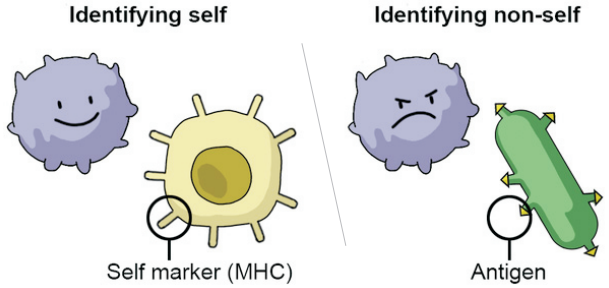


The third line of defence

When the number of pathogens is too great, and the two lines of defences of non-specific immunity have been broken through, the third line of defence of human body, i.e. the specific immunity will be activated. The specific immunity has a delayed response, but it is specific for each pathogen and a immunological memory will be developed.

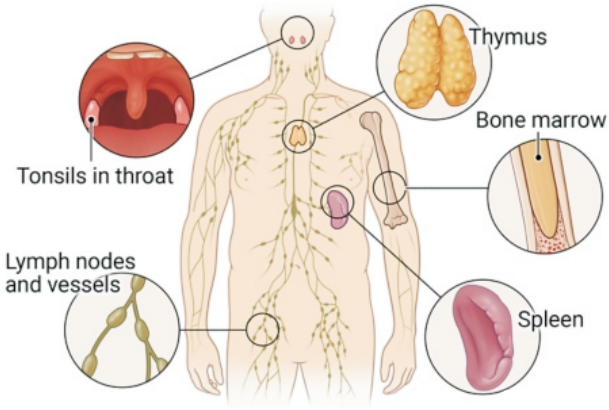
Recognition of non-self

The specific immunity are triggered by antigen. An antigen is any substance (generally foreign) that evokes an immune response. Antigen can binds to antibody and lymphocytes receptor protein.



Protiens, polysaccharides, glycoproteins signal the identity of the cell (host or forreign). A self (**MHC**-Major Histocompatability Complex) marker labels the body's cells as self or "friend".

An Antigen is a molecule, often on the surface of a pathogen, that the immune system recognizes as a specific "foe". Matching MHC markers is important when transplanting organs.



Organs of the specific immunity

Thymus
- Maturation of T-cells

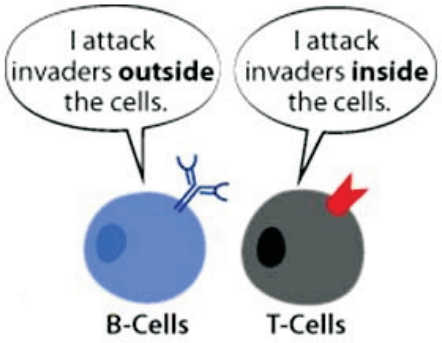
Bone marrow
- Production of new blood cells
- Maturation of B-cells

Spleen
- Filtering blood
- Removal old red blood
- Growing white blood cells

Lymph node
- Filtering blood
- Major site of specific immune response

Lymphocytes

The cells of the adaptive immune system are T and B lymphocytes. B cells and T cells are derived from the same hematopoietic stem cells, but they are developed in different organs. (B cells = bone marrow; T cells = thymus gland).



B cells are involved in the **humoral immune response**. B Lymphocytes produce antibodies that induce the immune system to respond to infection.

T cells are involved in the **cell-mediated immune responses**. T Lymphocytes recognize the particular infectious germs and remove them. There are different forms of T Lymphocytes.

Helper T-cells

T cells produce cytokines made of protein which respond to other white blood cells.

NK cells or Natural Killers

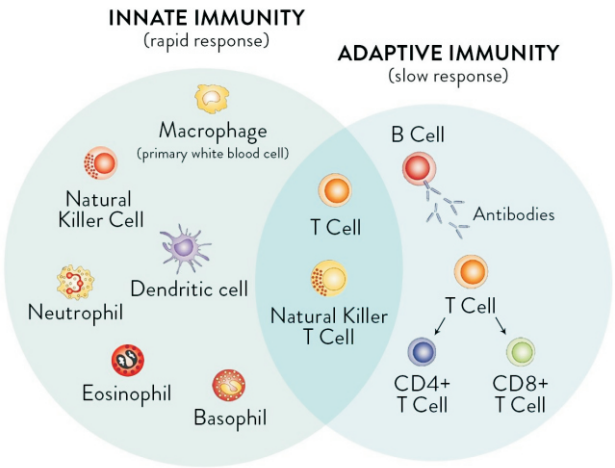
These killer cells are cytotoxic which attack and kill the infecting bacteria, virus or cancer infected cells.

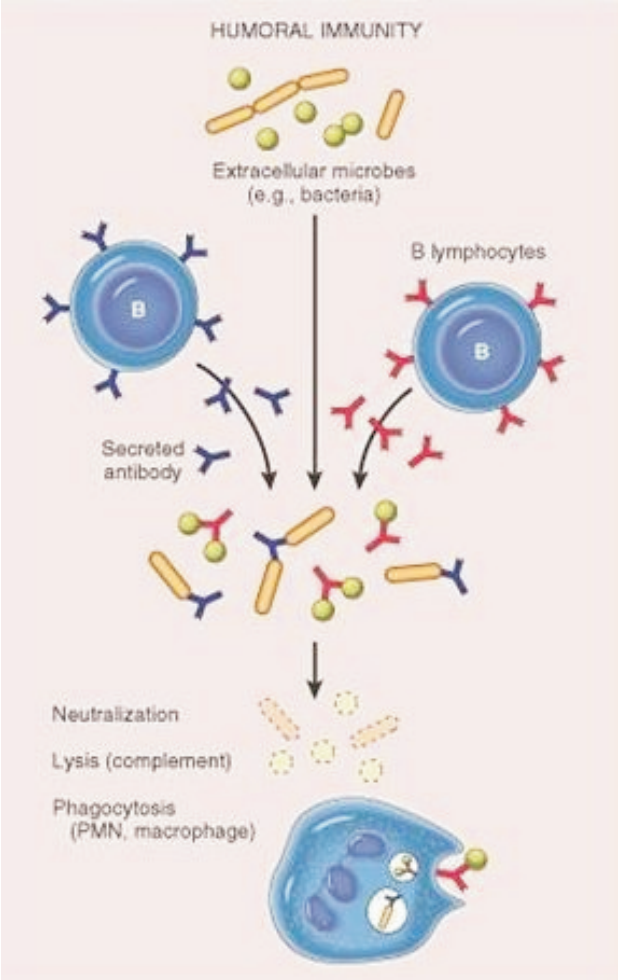
Memory T cells

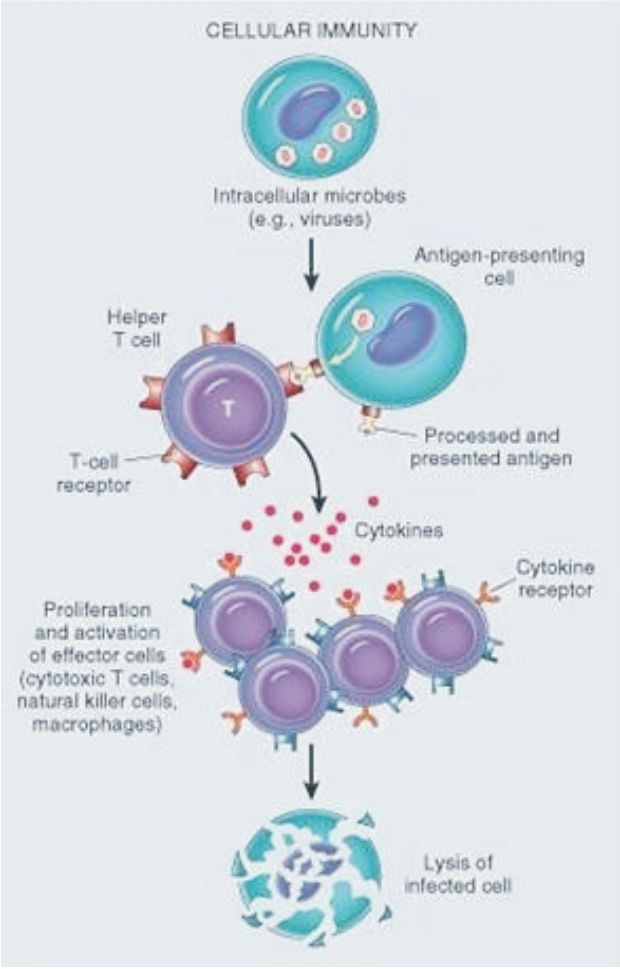
Memory T cells are stored to fight any future infection of the same kind of foreign pathogen.

Regulatory T cells

Regulatory T cells restrict the response of immune system to prevent auto immune diseases.







Humoral Immunity

Involves B-cell production of antibodies that bind antigens resulting in either Neutralization, Lysis (by complement system) or Phagocytosis and destruction.

Every B Cell has a different antibody that can only react to one specific antigen which are activated by T Helper Cells by secreating cytokines.
This causes the B cells to stimulate and divide (clonal selection and expansion) and differentiate into B plasma cells and B memory cells, these produce massive amounts of specific antibodies that will bing to their specific antigen.
Antibodies which are a type of B cell are also known as immunoglobulins which are Y-shaped proteins located on the surface of cells, viruses or bacteria, their role is to recognize and help remove foreign antigens. Every Antibody will recognize a specific foreign antigen due to the top of the 'Y' as they have a specific shape which allows antibodies to bind on a specific foreign antigen.
The 5 different B cells/Antibodies are IgG, IgM, IgA, IgE and IgD.

Cell-mediated Immunity

Involves T-cell recognition of abnormal antigens on the surface of host cells (indicating viral infection or tumorigenic change) and the killing of infected cells.
Cell-mediated immunity is an immune response that does not involve antibodies but involves T-cells.

Process: Macrophages engulf pathogens and presents antigens to the T cells. The antigen bind to a T cell receptor with the right specificity. The T cells was triggered, proliferates and differentiated into cytotoxic/killer T cells, helper T cells, regulatory/suppressor T cells and memory T cells.

Types of T cells

Cytotoxic/killer T cells (Tc cells)
- •Killing of infected cells by causing apoptosis (programmed cell death)
- • Release the cytotoxins perforin and granzymes.

Helper T cells (TH cells)
- • Maturation of B cells into plasma cells and memory B cells
- • Activation of cytotoxic T cells and macrophages

Regulatory/suppressor T cells
- • shut down T cell-mediated immunity toward the end of an immune reaction

Memory T cells
- • long-lived, quickly expand upon re-exposure to the same antigen

Adaptive Immunity

Natural Immunity (Naturally acquired)

An inherited characteristic by which all individuals of a species are immune to a certain disease. It is not induced by deliberate exposure.

Active Immunity

A person is exposed to a live pathogen, develops the disease, and then develops immunity and produce antibodies.
Effective and long lasting.

Antigens enter the body naturally, body induces antibodies and specialized lymphocytes

Passive immunization

Antibodies are acquired by another organisms.
- Fetus = placenta
- Infant = colostrum

Effective but short lived.

Antibodies pass from mother to fetus via placenta or to infant via the mother's milk

Artificial Immunity (Artificially acquired)

The body is given immunity to a disease by intentional exposure to small quantities of it.

Active Immunity

Vaccination
Long-lasting

Antigens are introduced in vaccines, body produces antibodies and specialized lymphocytes

Passive immunization

Not produced by the patients themselves
- Immuno-serum
- Short-lived

Preformed antibodies in immune serum are introduced by injection

Immunization

Administering Vaccines to prevent the disease is called immunization. This process of Immunization develops Artificial Active Acquired Immunity. Immunization through inoculation is a mass means of protecting a greater number of people against the spread of diseases.

Some of Immunization vaccines are,

BCG - Tuberculosis Vaccines
DPT - Diptheria, Pertussis, Tetanus Vaccine (Triple Antigen)
MMR - Mumps, Measels, Rubella
DT - Diptheria, Tetanus (Dual Antigen)
TT - Tetanus toxoid

Immune System Disorders

Immune system disorders develop when the immune system is either hyposensitive or hypersensitive.

When the immune system is less sensitive (hyposensitive) to an antigen, the response is unusually delayed or lessened in degree, causing diseases such as AIDS, cancer and other immune deficiency diseases.

When the immune system is too sensitive (hypersensitive) to an antigen, the response is activated when the body is healthy, leading to disorders such as allergy and autoimmune disorders (targeting self-antigen e.g. lupus, type I diabetes).

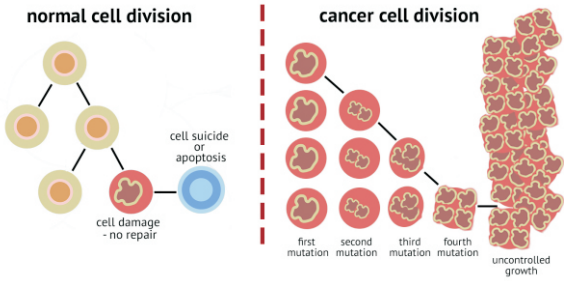
AIDS

AIDS (acquired immune deficiency syndrome) is caused by HIV (human immunodeficiency virus).
HIV harms the immune system by destroying the white blood cells (particularly CD4 cells, which are a type of immune cell called T cells) that fight infection. This puts one at risk for serious infections and certain cancers. AIDS is the final stage of infection with HIV.

HIV infects helper T cells, which undergoes programmed cell death. Due to this, B cells and cytotoxic T cells cannot be activated. The immune system is compromised. Individuals develop AIDS and often die from opportunistic infections.

Cancer

Cancer is an abnormal growth of cells with the potential to invade or spread to other parts of the body. Cancer occurs when a normal cell mutates. The cell evade the immune system and is not destroyed. The cell undergo unregulated growth that often form a mass or lump. Cancer cell enter the blood stream and spread to other parts of the body.



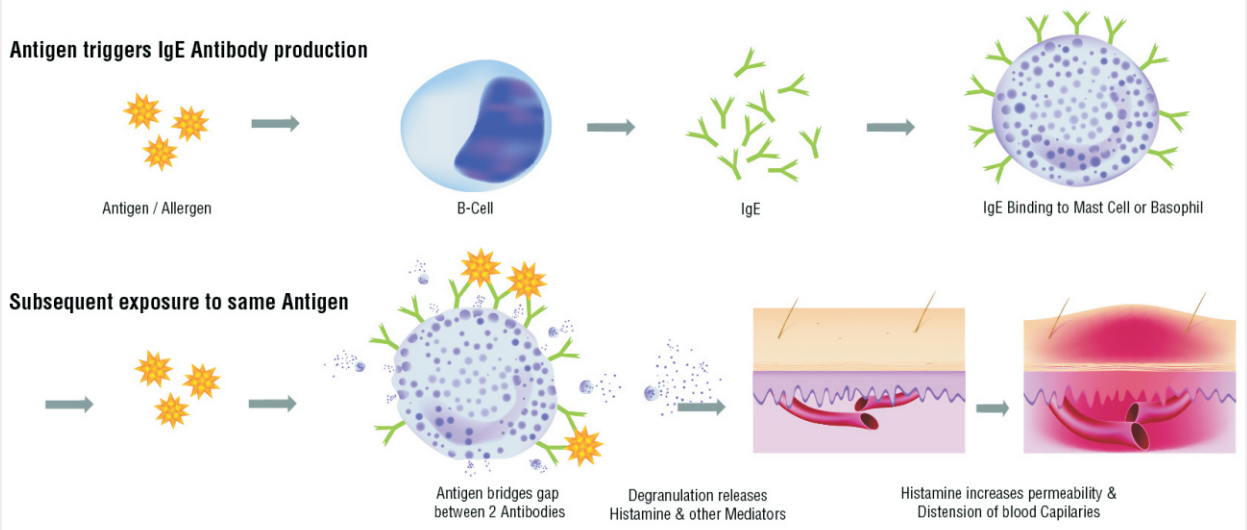
Allergies

An allergic reaction occurs when the immune system overreacts to a harmless substance known as an allergen. The immune system protects the body from infections, viruses and diseases. In some people, substances such as pollen, certain foods, latex, mold, pet dander, dust mites or insect stings are allergens that trigger the production of antibodies called Immunoglobulin E (IgE). These antibodies travel to cells that release chemicals, causing symptoms most often in the nose, lungs, throat, sinuses, ears, lining of the stomach or on the skin.

The first time a person with an allergy is exposed to the allergen, it may not cause a reaction. However, the person is then sensitized to the allergen can and even minor future exposures to this allergen produce an allergic reaction.

Allergies can affect anyone, regardless of age, gender, race, or socioeconomic status. Generally, allergies are more common in children. But a first-time occurrence can happen at any age. Or it can come back after many years of remission. Hormones, stress, smoke, perfume, or environmental irritants may also play a role in the development or severity of allergies.

Anaphylaxis (an-a-fi-LAK-sis) is a severe, life-threatening reaction involving multiple parts of the body to certain allergens.



When an allergic person encounter an allergen: B cells (plasma cells) produce antibodies to that allergen. The antibodies are attached on the mast cells under the skin or mucosa. When the person re-encounter the same allergen, the allergen will binds to the antibody on the mast cell, activating the mast cells. Mast cells release histamine. Histamine causes the dilation of blood capillaries, and the increase in the amount of blood flow, capillary permeability and tissue fluid. This causes itching, redness and hotness.

Infection and Disease

Infection occurs when a pathogen invades body cells and reproduces. Infection will usually lead to an immune response. If the response is quick and effective, the infection will be eliminated or contained so quickly that the disease will not occur.

Sometimes infection leads to disease. (Here we will focus on infectious disease, and define it as a state of infection that is marked by symptoms or evidence of illness.) Disease can occur when immunity is low or impaired, when virulence of the pathogen (its ability to damage host cells) is high, and when the number of pathogens in the body is great. Depending on the infectious disease, symptoms can vary greatly. Fever is a common response to infection: a higher body temperature can heighten the immune response and provide a hostile environment for pathogens. Inflammation, or swelling caused by an increase in fluid in the infected area, is a sign that white blood cells are on the attack and releasing substances involved in the immune response.

Viruses

Viruses are microscopic organisms that exist almost everywhere on earth. They can infect animals, plants, fungi, and even bacteria. Sometimes a virus can cause a disease so deadly that it is fatal. Other viral infections trigger no noticeable reaction. A virus may also have one effect on one type of organism, but a different effect on another. This explains how a virus that affects a cat may not affect a dog.

Viruses vary in complexity. They consist of genetic material, RNA or DNA, surrounded by a coat of protein, lipid (fat), or glycoprotein. Viruses cannot replicate without a host, so they are classified as parasitic. They are considered the most abundant biological entity on the planet.

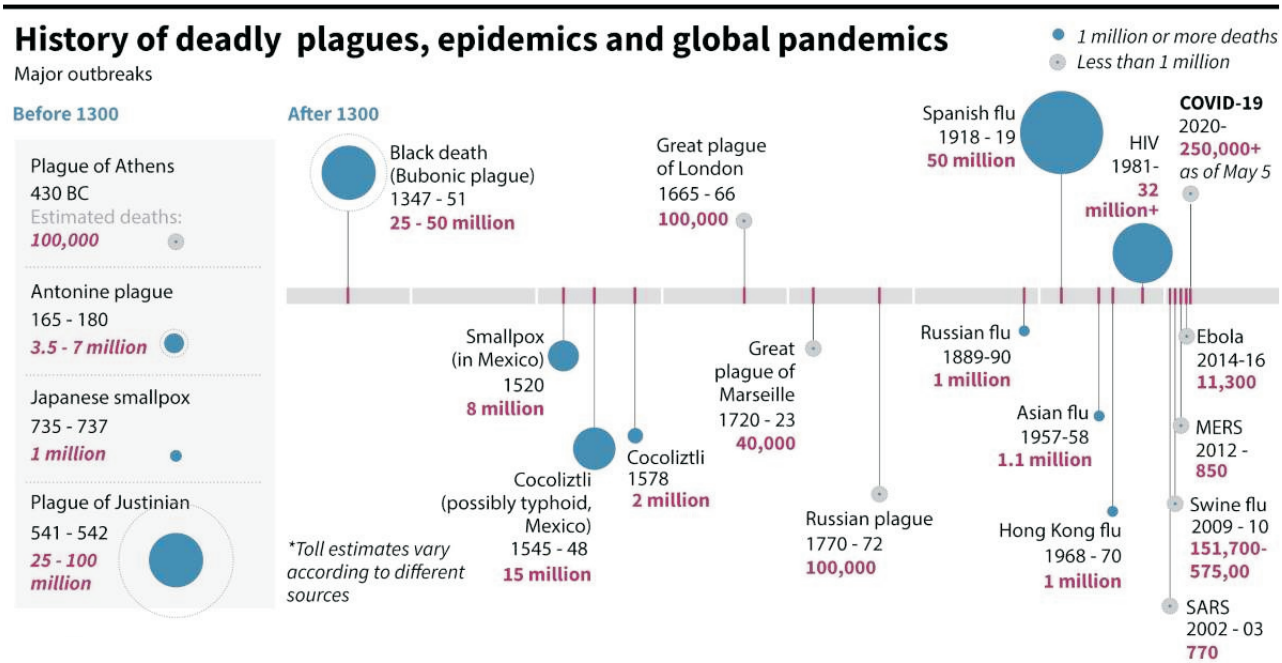
Fast facts on viruses

• Viruses are living organisms that cannot replicate without a host cell.
• There is no cure for a virus, but vaccination can prevent them from spreading.

Although scientists have learned much about the immune system, they continue to study how the body launches attacks that destroy invading microbes, infected cells, and tumors while ignoring healthy tissues. New technologies for identifying individual immune cells are now letting scientists quickly determine which targets are triggering an immune response. Improvements in microscopy are permitting the first-ever observations of B cells, T cells, and other cells as they interact within lymph nodes and other body tissues.

In addition, scientists are rapidly unraveling the genetic blueprints that direct the human immune response as well as those that dictate the biology of bacteria, viruses, and parasites. The combination of new technology and expanded genetic information will no doubt teach us even more about how the body protects itself from disease.

There are many viral diseases. Some, such as the common cold or the stomach flu, are minor and go away on their own within a few days. Others, however, are more serious. Cholera, bubonic plague, smallpox, and influenza are some of the most brutal killers in human history.



Invention of the Vaccine

Smallpox was widespread in the 18th century, and occasional outbreaks of special intensity resulted in a very high death rate. The disease, a leading cause of death at the time, respected no social class, and disfigurement was not uncommon in patients who recovered. The only means of combating smallpox was a primitive form of vaccination called variolation—intentionally infecting a healthy person with the "matter" taken from a patient sick with a mild attack of the disease. The practice, which originated in China and India, was based on two distinct concepts: first, that one attack of smallpox effectively protected against any subsequent attack and, second, that a person deliberately infected with a mild case of the disease would safely acquire such protection. It was, in present-day terminology, an "elective" infection—i.e., one given to a person in good health. Unfortunately, the transmitted disease did not always remain mild, and mortality sometimes occurred. Furthermore, the inoculated person could disseminate the disease to others and thus act as a focus of infection.

Jenner had been impressed by the fact that a person who had suffered an attack of cowpox—a relatively harmless disease that could be contracted from cattle—could not take the smallpox—i.e., could not become infected whether by accidental or intentional exposure to smallpox. Pondering this phenomenon, Jenner concluded that cowpox not only protected against smallpox but could be transmitted from one person to another as a deliberate mechanism of protection.

The story of the great breakthrough is well known. In May 1796 Jenner found a young dairymaid, Sarah Nelmes, who had fresh cowpox lesions on her hand. On May 14, using matter from Sarah's lesions, he inoculated an eight-year-old boy, James Phipps, who had never had smallpox. Phipps became slightly ill over the course of the next 9 days but was well on the 10th. On July 1 Jenner inoculated the boy again, this time with smallpox matter. No disease developed; protection was complete. In 1798 Jenner, having added further cases, published privately a slender book entitled An Inquiry into the Causes and Effects of the Variolae Vaccinae.

Vaccination rapidly proved its value, the procedure spread rapidly to America and the rest of Europe and soon was carried around the world. Jenner is often called a pioneer of immunization.

The second generation of vaccines was introduced in the 1880s by Louis Pasteur who developed vaccines for chicken cholera and anthrax, and from the late nineteenth century vaccines were considered a matter of national prestige, and compulsory vaccination laws were passed.

In the late 20th century, advances in laboratory techniques allowed approaches to vaccine development to be refined. Medical researchers could identify the genes of a pathogen (disease-causing microorganism) that encode the protein or proteins that stimulate the immune response to that organism. That allowed the immunity-stimulating proteins (called antigens) to be mass-produced and used in vaccines. It also made it possible to alter pathogens genetically and produce weakened strains of viruses. In that way, harmful proteins from pathogens can be deleted or modified, thus providing a safer and more-effective method by which to manufacture attenuated vaccines.

The twentieth century saw the introduction of several successful vaccines, including those against diphtheria, measles, mumps, and rubella. Major achievements included the development of the polio vaccine in the 1950s and the eradication of smallpox during the 1960s and 1970s. However, vaccines remain difficult for many important diseases, including herpes simplex, malaria, gonorrhea and HIV.

Edward Jenner, (17 May 1749 - 26 January 1823) was an English physician and scientist who was the pioneer of smallpox vaccine, the world's first vaccine.

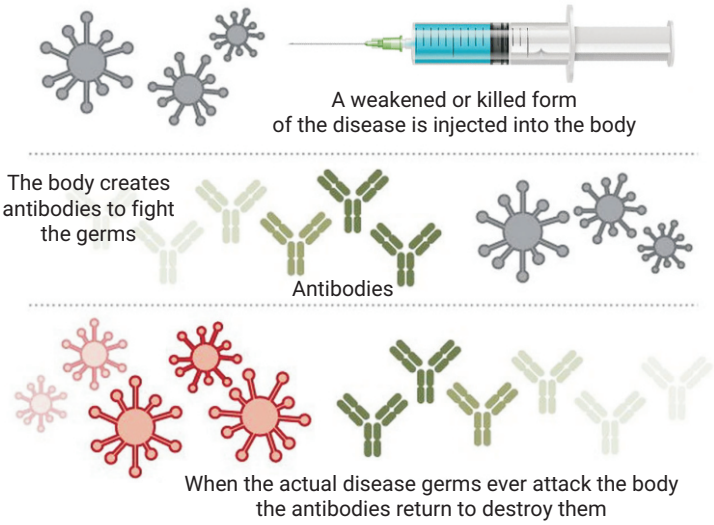
World Free of Smallpox

Almost two centuries after Jenner published his hope that vaccination could annihilate smallpox, on May 8, 1980, the 33rd World Health Assembly officially declared the world free of this disease. Eradication of smallpox is considered the biggest achievement in international public health.

How Vaccines works

A vaccine basically trains the immune system to recognize and attack the virus when it encounters it. Vaccines protect both the person who's vaccinated and the community. Viruses can't infect people who are vaccinated, which means vaccinated people can't pass the virus to others. This is known as herd immunity.

Vaccines harmlessly show viruses or bacteria (or even small parts of them) to the immune system. The body's defences recognise them as an invader and learn how to fight them.Then if the body is ever exposed for real, it already knows what to do. Vaccines are given to healthy people as prevention. Preventive vaccines don't treat or cure sickness – they prime your immune system to fight a potential disease.



Some types of vaccines and their groups

Whole-Pathogen

Live-attenuated
Uses a weakened form of the germ that causes a disease

Inactivated
Uses the killed version of the germ that causes a disease.

Subunit

Toxoid
Uses a toxin that creates immunity to the parts of the germ that cause a disease.

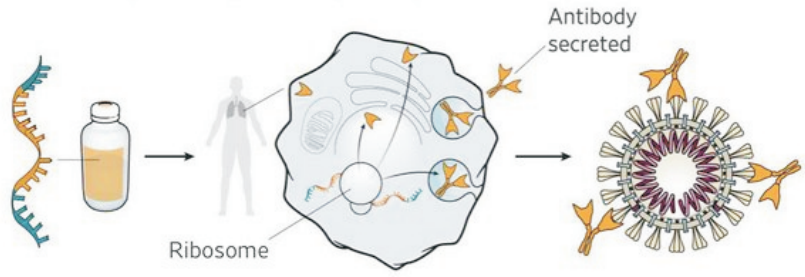
Nucleic Acid

Recombinant
Uses DNA from the targeted pathogen and inserts it into a different virus that has been rendered non-infectious.

DNA
Synthetic DNA instructs the cells to make proteins that resemble a pathogen. The body reacts by producing antibodies.

mRNA Vaccine

Work by introducing a 'messenger' RNA sequence (the molecule that tells cells what to build) which is coded for a disease specific antigen. Once produced within the body, the antigen is recognised by the immune system.



Vaccine
mRNA is encased in a lipid nanoparticle. After injection, gets into the body's cells.

Administration
The mRNA then instructs the cells to start making a protein that can be found on the virus.

Virus Inactivation
These proteins resemble the virus. They induce the body's immune system to make antibodies to the virus.

Phases in Development

Animal trials
These are primarily to demonstrate safety and to test the immune response generated by a vaccine. In some cases, this stage can be skipped altogether, but there may be safety trade-offs.

Phase I human trials
These are the first tests in people, usually involving 20 to 80 individuals and are used to demonstrate safety and ensure any side effects aren't too severe.

Phase II human trials
This requires larger groups of people and is used to test efficacy. Some vaccines can skip from here to regulatory approval when there is urgent need.

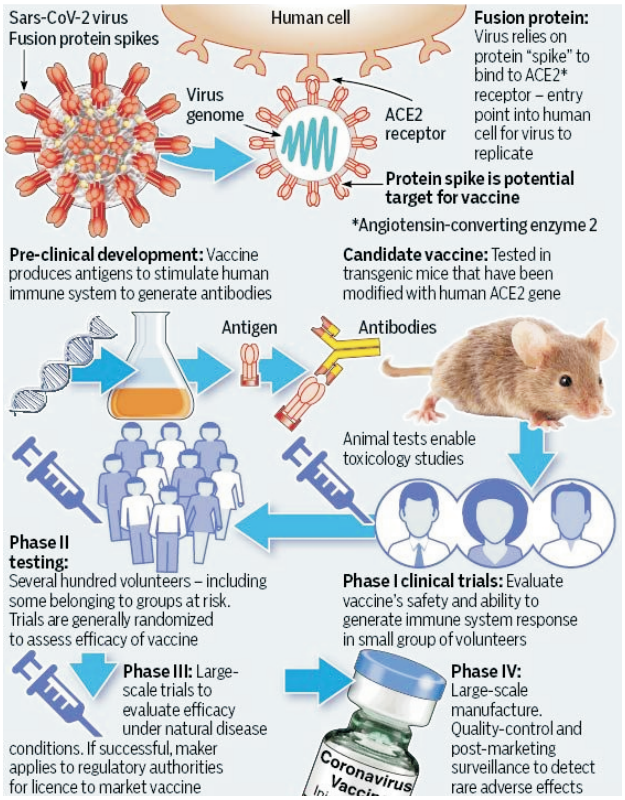
Phase III human trials
At this stage, a new vaccine is tested on hundreds to thousands of people, to clearly evaluate both efficacy and safety.

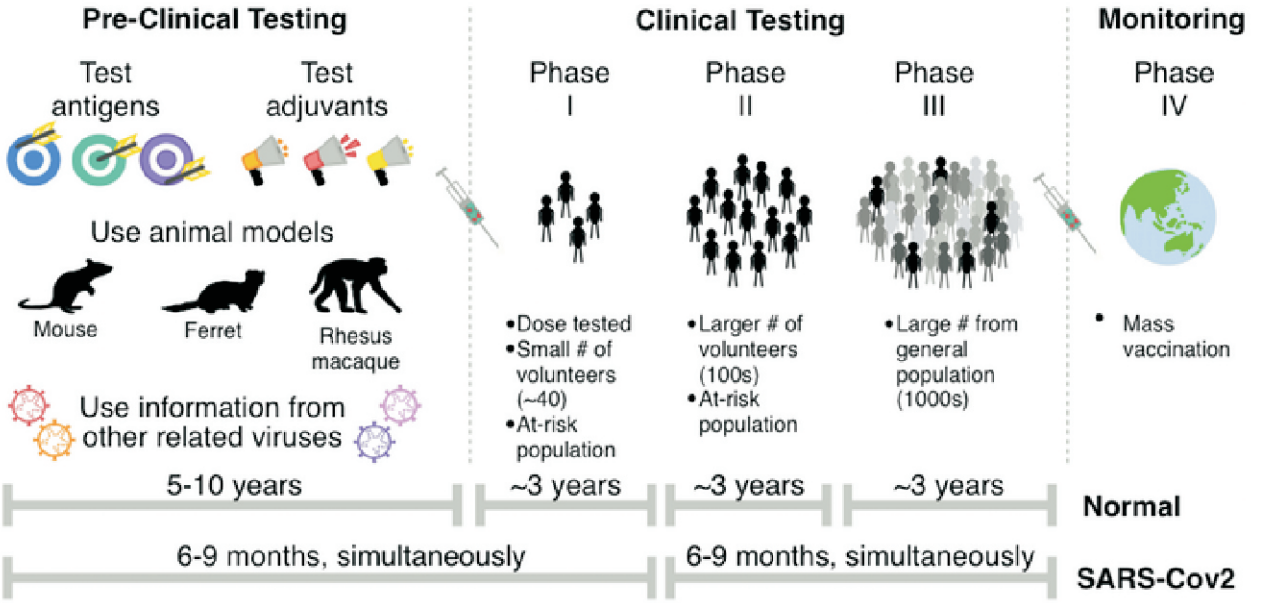
Regulatory approval
After examining clinical trial evidence, regulatory bodies determine whether the vaccine can be licensed for public use. This may come with the requirement that follow-up safety data be gathered.

Mass production
At this point, manufacturing of a vaccine is ramped up under strict quality control and consistency standards.

Public access
When the new vaccine becomes available, governments and public health authorities have to determine which groups of people get it first.

Vaccine development involves lot of challenges, striking the balance between speed and safety is always going to be a challenge. If a vaccine takes too long to develop, the initial outbreak may be over, which creates its own set of problems. For example, by the time clinical trials of an Ebola vaccine were under way during a large outbreak that began in West Africa in 2014, disease transmission had slowed so much that researchers couldn't treat enough people to gather the robust data needed for regulatory approval. Only after a larger outbreak and a bigger trial was there enough evidence to prove safety and efficacy. Vaccine for Ebola "Ervebo" was finally approved by the European Medicines Agency in November 2019.
Below is expected time line for Sars-CoV-2





Factors that hinder immunity

Malnutrition: It is a condition of severe nutrients deficiency resulting from insufficient intake of essential vitamins, minerals and macronutrients (a very low calorie intake resulting in being underweight). It can also occur due to a high calorie intake lacking essential vitamins and minerals resulting in being overweight yet malnourished or due to certain diseases which result in malabsorption (improper absorption) of nutrients. In such cases the person remains malnourished even after consuming a highly nutritious diet. The lack of essential nutrients weakens our immune system. Malnutrition during childhood can impair the development of thymus which can lead to lifetime immunity damage.

High calorie intake: Consuming too many calories results in being obese or overweight. Obesity hinders the function of immune system. This causes a weakened initial response to pathogens and impaired immune cell proliferation. Evidences show that in 2009 influenza A (HIN1) pandemic, obese individuals had higher morbidity and mortality rates than those of non obese individuals.

Low calorie intake: Severe caloric restriction may decrease the production of lymphocytes. Therefore, it is important to consume optimal amounts of calories and nutrients. Optimal nutrition level varies from individual to individual. It depends upon a number of factors like age, gender, genetics, body composition, physical activity levels, etc.

Excessive salt intake: In a 2020 pilot study, participants consumed 6 grams of salt in addition to their daily salt intake. After a period of 1 week it was observed that the disease fighting ability of neutrophils taken from these individuals was reduced. This study implies that a high salt intake can reduce the ability of our immune cells to fight infections. Currently the World Health Organization (WHO) recommends consuming less than 5 grams of salt per day.

Dysbiosis: It is a condition in which there is an imbalance in the gut microbiome. Gut bacteria signals to both innate and adaptive immune systems and produce short-chain fatty acids (SCFAs) which help in immune cells functioning. Gut bacteria also regulate the activity of lymphocytes. Dysbiosis can therefore lead to impaired immunity and it can also provide room for the growth of infectious bacteria.

Alcohol consumption: Alcohol consumption has a detrimental impact on the functioning of important immune cells including macrophages and lymphocytes. It also decreases the production and function of cytokines. Cytokines play a major role in initiating the immune response.

Immune supporting nutrients

Good nutrition is essential to a strong immune system, which may offer protection from seasonal illness and other health problems. No one food or supplement can prevent illness but you may help support your immune system by including these nutrients in your overall eating plan on a regular basis.

Protein plays a role in the body's immune system, especially for healing and recovery. Eat a variety of protein foods including seafood, lean meat, poultry, eggs, beans and peas, soy products and unsalted nuts and seeds.

Vitamin A helps regulate the immune system and protect against infections by keeping skin and tissues in the mouth, stomach, intestines and respiratory system healthy. Get this vitamin from foods such as sweet potatoes, carrots, broccoli, spinach, red bell peppers, apricots, eggs or foods labeled "vitamin A fortified," such as milk or some cereals.

Vitamin C supports the immune system by stimulating the formation of antibodies. Include more sources of this healthy vitamin by choosing citrus fruits such as oranges, grapefruit and tangerines, or red bell pepper, papaya, strawberries, tomato juice or foods fortified with vitamin C, such as some cereals.

Vitamin E works as an antioxidant and may support immune function. Include vitamin E in your diet with fortified cereals, sunflower seeds, almonds, vegetable oils (such as sunflower or safflower oil), hazelnuts and peanut butter.

Zinc helps the immune system work properly and may help wounds heal. Zinc can be found in lean meat, poultry, seafood, milk, whole grain products, beans, seeds and nuts.

Fluids and Electrolytes: Consuming adequate fluids (water) and electrolytes such as sodium, potassium and chloride help regulate the body's temperature. Sick people need to drink extra fluids to keep from dehydrating.

People who are at the highest risk for compromised immune health are those who do not get adequate amounts of food in their diets, do not have access to foods with key nutrients, are malnourished, or have certain health conditions that may require additional nutrition support.

Sometimes it's hard to get enough of all the immune system supporting nutrients you need from your diet alone, speak with a registered nutritionist to help you in finding right supplements.

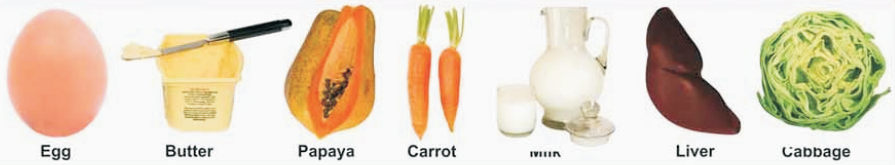
Healthy Food Chart

VITAMIN A (FAT SOLUBLE)

FOR

Normal Growth and Development, Normal Night Vision & Healthy Epithelium, Anti-infective.

Deficiency leads to :
Retarded Growth, Night Blindness, Diseased Epithelium, Dry Scaly Skin, Colds, Bronchitis, Diarrhoea, Xerophthalmia.



VITAMIN B1 (VITAMIN F) (WATER SOLUBLE)

FOR

Growth, Appetite, Normal Intestinal Function, Nerve and Muscle Function.

Deficiency leads to :
Beriberi, Loss in Weight, Loss of Appetite, Enervation, Defective Carbohydrate Metabolism.

VITAMIN B2 (VITAMIN G) (WATER SOLUBLE)

FOR

Growth, Healthy Skin, Mouth & Eyes.

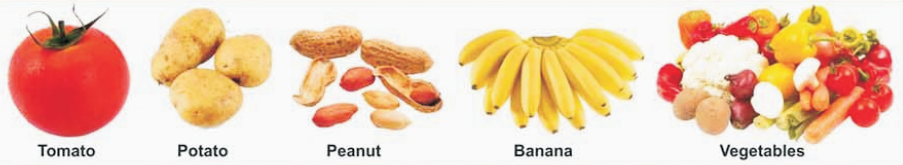
Deficiency leads to :
Retarded Growth, Dim Vision, Photophobia, Keratitis, Blistered Tongue, Premature Senility.

VITAMIN B (P.P. FACTOR) (WATER SOLUBLE)

FOR

Proper Carbohydrate Metabolism, Nervous System.

Deficiency leads to :
Pellagra, Glossitis, Dermatitis, Psychosis, Diarrhoea.



VITAMIN B6 (WATER SOLUBLE)

FOR

Proper Metabolism of Amino Acids, Disease-Resistance, Anti-Emetic.

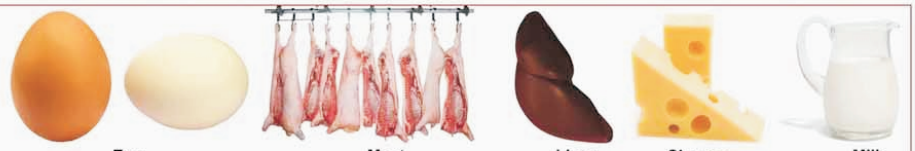
Deficiency leads to :
Anaemia, Atrophic Lymph Tissues, Poor Resistance against Diseases.

VITAMIN B12 (WATER SOLUBLE)

FOR

Red Blood Cells, Nitrogen Metabolism, Healthy, Nervous Tissue.

Deficiency leads to :
Pernicious Anaemia.

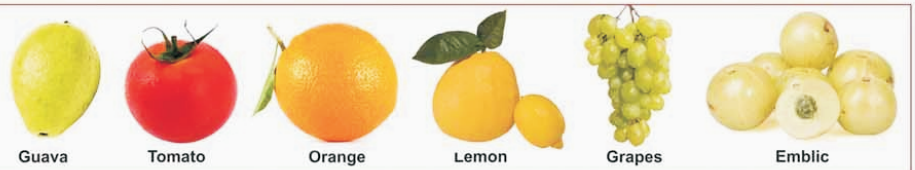


VITAMIN C (WATER SOLUBLE)

FOR

Healthy Growth, Good Gum & Teeth, Sound Blood Vessels, Rapid Healing, Resistance against Flu & Colds.

Deficiency leads to :
Scurvy Swollen Gums, Bursting of Blood Capillaries.



VITAMIN D (FAT SOLUBLE)

FOR

Proper Utilisation of Calcium & Phosphorus Formation of Bones and Teeth.

Deficiency leads to :
Rickets, Poor Growth, Weak Teeth & Bones Tooth Decay.

VITAMIN E (FAT SOLUBLE)

FOR

Normal Reproduction.

Deficiency leads to :
Sterility, Muscular Paralysis.

VITAMIN K (FAT SOLUBLE)

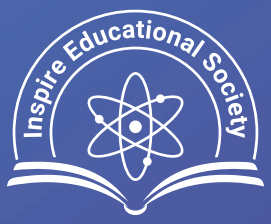
FOR

Normal Blood Coagulation, and Liver Functioning.

Deficiency Leads to :
Haemorrhage.

“ Life is in an equilibrium state between synthesis and degradation of proteins ”

- Yoshinori Ohsumi



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